REMARKS

Introductory Comments

Reconsideration of the above-identified application in view of the above amendments and foregoing arguments is respectfully requested.

Claims 31-54 are pending and under consideration. Claims 22 and 23 have been deleted. Claims 31, 34, 36, 38, 43, 46 and 50 have been amended. Claims 34, 36 and 46 have been amended to correct obvious typographical errors. Claims 43, 46 and 50 have been amended to correctly recite "complements thereof" instead of "degenerate codon equivalents thereof". Support for this amendment can be found on page 4, line 32 to page 5, line 2. Additionally, claims 31, 34, 38, 43, 46 and 50 have been amended as discussed below. No new matter has been added as a result of these amendments.

Claim Objection

Claim 36 is objected to because the claim recites "dectectioin" which is a typographical error. The claim has been amended to correct the typographical error by reciting "detection" instead. Withdrawal of the objection to claim 36 for this informality is respectfully requested.

Rejection of Claims 22-23 and 31-54 Under 35 U.S.C. § 112, Second Paragraph

Claims 22-23 and 31-54 are rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. Specifically, the Examiner asserts that the omitted step is the detection used for the claimed invention and that it is unclear from the claims as to the type of detection method being employed. Additionally, the Examiner states that there are many different detection steps that are encompassed by the claims such as hybridization, column chromatography, and *in situ* RT-PCR hybridization. The Examiner finally asserts

that "these steps are need [sic] for one of skill in the art to practice because conditions such as hybridization parameters, have not been provided so that one of skill could practice the invention without uncertainty." Applicants respectfully traverse the rejection.

As noted above, claims 22 and 23 have been deleted.

Applicants submit that the claims are clear and recite a "detection step". Claims 31 and 43 recite a detection of step of "(b) detecting the presence of said target polynucleotide", claims 34 and 46 recite a detection step of "(c) detecting the presence of said amplicon", and claims 38 and 50 recite a detection step of "(c) detecting said second stage reaction product". As noted by the Examiner, there are different types of detection such as hybridization, column chromatography and *in situ* RT-PCR hybridization. The claims do not recite a specific type of detection but are intended to cover all types of detection. The claims, however, require the detection to use the specific polynucleotides or oligonucleotides as claimed.

The specification clearly defines these types of detection and indicates that one of ordinary skill in the art would be able to recognize and appreciate the parameters required for each particular type of detection. For example, on page 23, lines 5-7, it is stated that the polynucleotides will hybridize to sequences if there is at least 50% identity between the polynucleotide and the sequences. Other types of detection may be used such as fluorescent *in situ* hybridization (FISH) (page 24, lines 8-18 and page 61, lines 15 to page 62, line 9), general hybridization (page 57 line 19 to page 58, line 31, page 59, line 5-10 and page 60, line 21 to page 61, line 13), amplification (PCR, LCR, NASBA, SDA, RCR and TMA) (page 26, lines 1-15, page 29, lines 4-20 and page 31, lines 1-11) and heterogenous and homogeneous detections (page 26, lines 16-28 and page 27, lines 19-32). Applicants have cited literature references describing these various types of detection and have provided examples throughout the specification describing the parameters used in these types of detection. Therefore, Applicants submit that the specific types of detection using various parameters

specific for each type of detection are not considered essential steps within the methods as claimed.

Accordingly, Applicants respectfully request withdrawal of the rejection of claims 31-54 under 35 U.S.C. § 112, second paragraph.

Rejection of Claims 22-23 and 31-54 Under 35 U.S.C. § 112, First Paragraph

Claims 22-23 and 31-54 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner states that (A) there does not appear to be an adequate written description in the specification of the essential structural feature of all the possible target sequence that will be detected when using the purified polynucleotides of SEQ ID NOS: 1, 4, 5, 8 and 10, (B) because the claims as currently interpreted have not set forth the conditions for said detection method nor has the claimed invention set forth any specific detection step, any sequence that would bind to said purified sequences by normal base pairing would be detected and as such would encompass an extensive number of sequences that are found within the test sample, and (C) Applicants do not appear to have reduced to practice the detection of all target sequences that are capable of binding to the purified sequence of SEQ ID NOS: 1, 4, 5, 8 and 10 and Applicants have not provided a sufficient written description of any structure that may be correlated with target sequence of urinary tract tissue gene UT116 that may be detected as a target sequence. With respect to the Examiner's argument (C), the Examiner further states that "[a] 'target polynucleotide' sequence encompass *any* nucleic acid sequence that is able to hybridize to any one of the purified SEQ ID numbers claims [sic] under any hybridization condition found within the test sample. Thus the genus compounds encompassed by this term is extensive and the artisan would not be able to recognize that Applicant was in possession of the invention as now claimed. In addition, as noted *supra* because

the method steps have not been outlined, such as hybridization conditions, one of skill in the art would not be able to determine whether the applicant was in possession of all the possible target nucleotide sequence detected within the sample." Applicants respectfully traverse the rejection.

Applicants traverse the Examiner's argument (A) above, that there does not appear to be an adequate written description in the specification of the essential structure feature of all the possible target sequence that will be detected when using the purified polynucleotides of SEQ ID NOS: 1, 4, 5, 8 and 10. As stated above, the specification on page 23, lines 5-7, states that the polynucleotides will hybridize to sequences if there is at least 50% identity between the polynucleotide and the sequences. The present claims are drawn to a method of detecting target polynucleotides and not the target polynucleotides themselves. Applicants submit that the specification provides an adequate written description with respect to the target polynucleotides as the claims are drawn to a method of detecting the target polynucleotides and not the target polynucleotides themselves.

Applicants traverse the Examiner's argument (B) above, that because the claims as currently interpreted have not set forth the conditions for said detection method nor has the claimed invention set forth any specific detection step, any sequence that would bind to said purified sequences by normal base pairing would be detected and as such would encompass an extensive number of sequences that are found within the test sample. As noted above, the claims are not required to recite a specific type of detection since the claims are intended to cover all types of detections. Applicants' arguments *supra* are incorporated herein. Applicants have surprisingly discovered that the purified polynucleotides comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 1-12, and complements thereof are useful in a method of detecting the presence of a target polynucleotide in a test sample. The presence of the target polynucleotide is useful as an indicator for urinary tract diseases. As noted above, Applicants' claims are drawn to a method of detecting target polynucleotides and not to the target polynucleotides themselves and therefore,

even if the detection method as claimed covers many polynucleotides as the Examiner suggests, the method of detecting the target polynucleotides itself is adequately disclosed in the specification since the invention is based on the usefulness of SEQ ID NOS: 1-12, and complements thereof and the parameters used are based on the type of detection.

Applicants traverse the Examiner's argument (C) above, that Applicants do not appear to have reduced to practice the detection of all target sequences that are capable of binding to the purified sequence of SEQ ID NOS: 1, 4, 5, 8 and 10 and Applicants have not provided a sufficient written description of any structure that may be correlated with target sequence of urinary tract tissue gene UT116 that may be detected as a target sequence. The Examiner also states that "[a] 'target polynucleotide' sequence encompass [sic] *any* nucleic acid sequence that is able to hybridize to any one of the purified SEQ ID numbers claims [sic] under any hybridization condition found within the test sample. Thus the genus compounds encompassed by this term is extensive and the artisan would not be able to recognize that Applicant was in possession of the invention as now claimed. In addition, as noted *supra* because the method steps have not been outlined, such as hybridization conditions, one of skill in the art would not be able to determine whether the applicant was in possession of all the possible target nucleotide sequence detected within the sample."

As noted above, the types of detection of target polynucleotides is well documented and described in the specification. As noted by the Examiner, a target polynucleotide sequence encompasses any nucleic acid sequence that is able to hybridize to any one of the purified SEQ ID numbers as claimed. However, as discussed *supra*, these target polynucleotides will hybridize to sequences if there is at least 50% identity between the polynucleotide and the sequences (page 23, lines 5-7). It is the use of the claimed SEQ ID NOS in order to determine what the target polynucleotides are that is being claimed as the claims are directed to a method of detection.

The significance of the claimed SEQ ID NOS, which are derived from the UT116 gene, is well described in the specification. On page 11, lines 23 to page

12, line 7, it is disclosed that the compositions and methods of the invention will enable the identification of markers indicative of urinary tract tissue disease or condition. The nucleotide sequences contain open reading frames from which an immunogenic epitope may be found. The epitope is believed to be unique to the disease state or condition associated with UT116. The uniqueness of the epitope may be determined by its immunological reactivity and specificity with antibodies directed against proteins and polypeptides encoded by the UT116 gene and its nonreactivity with any other tissue markers. The detection of a product by using the claimed polynucleotide sequences is indicative of the presence of UT116 mRNAs, and suggests a diagnosis of urinary tract disease or condition (page 58, line 28 to page 61, line 13). Table 1 on page 59 shows ribonuclease protection results from a methodology using the polynucleotides of the invention to identify bladder cancer. Figure 3 shows the results of an analysis of UT116 hybridization to a Northern blot containing normal bladder tissue and bladder cancer tissues. The UT116 probe detected an approximately 1.0 kb RNA in four normal bladder samples (lanes 1-4) and two bladder cancer tissues (lanes 8 and 9). Lane 12, containing the positive control RNA isolated from *E. coli* containing a UT116 plasmid, was also positive for the UT116 hybridization. Example 6 on pages 60 and 61 of the specification provides an example of how the dot and blot assay can be used to evaluate the presence of target nucleic acid sequences as an indication of the presence of UT116, suggesting a diagnosis of a urinary tract tissue disease or condition.

Applicants submit, therefore, that the specification provides an adequate written description of the invention under 35 U.S.C. § 112, first paragraph. For these reasons, Applicants respectfully request withdrawal of the rejection of claims 31-54 under 35 U.S.C. § 112, first paragraph.

Additionally, claims 31-54 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention based on the following reason.

Specifically, the Examiner states that since the claims recite the phrase "is selected from a group consisting of", it is not clear to one of ordinary skill in the art that at the time of filing the Applicant was in possession of the claimed invention because the polynucleotides encompassed are not described. The Examiner also states "Although it is clear that the group consists of SEQ ID NOS: 1, 3, 5, 8 and 10, applicant has not conveyed to one of skill in the art that applicant was in possession of polynucleotides which read on any sequence found within SEQ ID NOS: 1, 4, 5, 8 or 10 (because of the open interpretation of the word 'is')". Applicants have amended the claims to delete "is" and recite the well-accepted term "comprise". Applicants fully traverse the Examiner's rejection for the following reasons.

The inquiry into whether the description requirement is met is determined on a case-by-case basis and is a question of fact. Section 2163 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). When a question regarding the adequacy of the written description arises, the fundamental factual inquiry is whether the specification conveys to those skilled in the art, as of the filing date sought, that applicant was in possession of the invention being claimed. Section 2163.02 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). Possession can be shown in a number of ways. For example, an Applicant can show possession by: (1) an actual reduction to practice of the claimed invention; (2) a clear depiction of the invention in detailed drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention; or (3) any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Id.*

A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption. Section 2163.04 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). The Examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. *Id.* The Examiner has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention as defined by the claims. *Id.* "A general allegation of unpredictability in the art is not a sufficient reason to support a rejection for lack of adequate written description." *Id.* The *Manual of Patent Examining Procedure* even cautions Examiners that "rejection of an original claim for lack of written description should be rare." (See Section 2163 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003)).

The U.S. PTO has issued Guidelines governing its internal practice for assessing whether the specification contains an adequate written description of the invention being claimed. In its Guidelines, the PTO has determined that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics..., i.e., the complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, January, 2001 *Guidelines*, 66 Fed. Reg. at 1106.

Contrary to the arguments made by the Examiner, Applicants submit that the specification adequately describes the polypeptides encompassed within the scope of the invention being claimed. First, as specifically recommended by the *Guidelines*, Applicants have provided the complete structure of the claimed polypeptides as demonstrated in SEQ ID NOS: 1-12. Second, with respect to the issue raised by the Examiner regarding the numerous structural variants of the claimed sequences, Applicants submit that because the level of skill in the area of molecular biology is considerably high, one of ordinary skill in the art, after

reviewing Applicants specification, would clearly recognize that the Applicants have provide an adequate written description of the variants, substitutions, deletions and/or additions encompassed by the claims. Applicants specifically direct the Examiner's attention to page 23, line 33 to page 24, line 7 of the specification where it states that "Thus a polypeptide of the present invention may have an amino acid sequence that is identical to that of the naturally occurring polypeptide or that is different by minor variations due to one or more amino acid substitutions. The variation may be a "conservative change" typically in the range of about 1 to 5 amino acids, wherein the substituted amino acid has similar structural or chemical properties, e.g., replacement of leucine with isoleucine or threonine with serine. In contrast, variations may include nonconservative changes, e.g., replacement of a glycine with a tryptophan. Similar minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which and how many amino acid residues may be substituted, inserted or deleted without changing biological or immunological activity may be found using computer programs well known in the art, for example, DNASTAR software (DNASTAR Inc., Madison, WI)." As illustrated by the above cited portion of the specification, computer programs are available to those of ordinary skill in the art and these programs can be used in providing guidance in determining "which and how" many amino acids residues in polypeptides that can be substituted, inserted or deleted. The use of such programs is well-known to those of ordinary skill in the art for both polypeptides and polynucleotides. Variants of the polynucleotides of the present invention are also well-described in the specification as follows.

On page 22, lines 4-11, the specification states "The polynucleotide may be in the form of RNA or DNA. Polynucleotides in the form of DNA, cDNA, genomic DNA, nucleic acid analogs, and synthetic DNA are within the scope of the present invention. The DNA may be double-stranded or single-stranded, and if single-stranded, may be the coding (sense) strand or non-coding (anti-sense) strand. The coding sequence which encodes the polypeptide may be identical to the coding sequence provided herein or may be a different coding sequence

which coding sequence, as a result of redundancy or degeneracy of the genetic code, encodes the same polypeptide as the DNA provided herein."

Finally, on page 22, lines 17-21, the specification states "In addition, the invention includes variant polynucleotides containing modifications such as polynucleotide deletions, substitutions or additions, and any polypeptide modification resulting from tee variant polynucleotide sequence. A polynucleotide of the present invention also may have a coding sequence which is a naturally occurring allelic variant of the coding sequence provided herein."

Therefore, in view of the aforementioned arguments, Applicants submit that one of ordinary skill in the art would clearly recognize that Applicants had possession of the claimed invention and have provided an adequate written description. Thereupon, Applicants respectfully submit that the Examiner has failed to provide sufficient factual evidence to rebut the presumption that the description as filed is inadequate. Moreover, the Examiner fails to present any factual evidence as to why a person of ordinary skilled in the art would not recognize in Applicants disclosure a description of the invention as defined by the claims. In view of the absence of such evidence, Applicants submit that this rejection should be withdrawn.

Accordingly, Applicants respectfully request withdrawal of the rejection of claims 31-54 under 35 U.S.C. § 112, first paragraph.

CONCLUSION

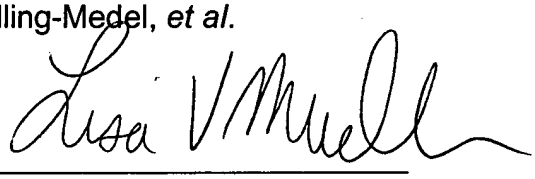
Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. § 112. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, he is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge deposit account no. 23-0785.

Respectfully submitted,

Billing-Medel, *et al.*



Lisa V. Mueller
Registration No. 38,978
Attorney for Applicants

Wood, Phillips, Katz, Clark & Mortimer
500 West Madison Street
Suite 3800
Chicago, IL 60662-2511

Tel.: (312) 876-2109
Fax.: (312) 876-2020